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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/043,344	LOOSMORE ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed July 16, 2004 has been entered. Claims 1-13 and 15-17 have been cancelled. Claim 14 has been amended. Claims 18-27 have been newly added. Claims 14 and 18-27 and SEQ ID NO:74 are under consideration in this office action.

Specification

2. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

3. The disclosure is objected to because of the following informalities: at page 44 of the instant specification the American Type Culture Collection address cited in the specification is no longer correct. Effective 23 March 1998, the correct address is 10801 University Boulevard, Manassas, VA 20110-2209. Appropriate correction is required.

Claim Objections

4. Claim 24 is objected to since the claims shall not, except where absolutely necessary, rely, in respect of the technical features of the invention, on references to the description, tables or drawings. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 14 and 18-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims are drawn to an immunogenic composition comprising a synthetic peptide having no less than six amino acids and no more than 150 amino acids and containing an amino acid sequence corresponding to a portion of a transferring receptor protein of a strain of bacteria or an analog of the transferrin receptor protein and a pharmaceutically acceptable carrier with at least one active component producing an immune response when administered to a host.

The written description in this case only sets forth specific amino acid sequences and does not disclose a particular portion of the protein or analogs of the transferrin receptor protein, therefore the written description is not commensurate in scope with the claims drawn to portions or analogs of the transferrin receptor protein. Neither the specification nor the claims teach how to define the portion or analogs. Neither the claims nor the specification teach how to obtain such portions or analogs. There is no guidance as to what the portions or analogs are; or what portions or analogs can or cannot be used in the immunogenic composition being claimed. The specification does not include structural examples of the analogs. Thus, the resulting portion or analog comprised within the immunogenic composition could result in compositions not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Without knowing a protein's three dimensional structure there is no reliable method for determining which linear segments of the protein are accessible to the host's immune system and regardless of whether the three dimensional structure is known or not, short linear peptides often appear not to have the ability to mimic the required secondary and tertiary conformational structures to constitute appropriate immunogenic and antigenic determinants. Consequently one of skill in the art would be forced into excessive

experimentation to identify which portions or analogs are able to invoke an immune response.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically named amino acid sequences, the skilled artisan cannot envision the detailed structure of the portions or analogs of the transferring receptor protein, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. Furthermore, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement that defines a genus only by their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus. Therefore, only the recited and claimed amino acid sequences and not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

6. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This is a deposit rejection.

The specification lacks complete deposit information for the deposit of non-typeable *Haemophilus influenzae* strains PAK12085, SB12m SB29, SB30, SB32 and SB33. It is not clear that cell lines possessing the properties of non-typeable

Haemophilus influenzae strains PAK12085, SB12m SB29, SB30, SB32 and SB33 are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of non-typeable *Haemophilus influenzae* strains PAK12085, SB12m SB29, SB30, SB32 and SB33, a suitable deposit for patent purposes is required. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell line is an unpredictable event.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.

If the deposit has not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are

required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to

corroborate that the non-typeable *Haemophilus influenzae* strains PAK12085, SB12m SB29, SB30, SB32 and SB33 strains described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

7. Claims 14 and 18-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the limitation "said at least one active component" in the claim. There is insufficient antecedent basis for this limitation in the claim.

8. Claim 14 is vague and confusing because it is unclear what is meant by the phrase "...corresponding to a portion of a transferring receptor protein of a strain or of an analog..."(see 112, first paragraph rejection). The claim as written fails to clearly define the synthetic protein. The mention of the claimed peptide's potential number of amino acids comprised within it does not adequately define the peptide.

9. The term "analog" in the claim is a relative term that renders the claim indefinite. The term "analog" is not defined by the claim, the specification does not provide a

standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Thus the metes and bounds of the term are vague and it is unclear what proteins or peptides would or would not be considered analogs. Thus clarification is required to overcome the rejections.

10. Claim 14 is vague and indefinite as it is unclear what is encompassed by "at least one active component". What components are intended to be included in this composition? Appropriate clarification is required to overcome the rejection.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 14,18-19 and 24-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 5,922,562 in view of Loosmore et al., WO 96/40929. Although the conflicting claims are not identical, they are not patentably distinct from each other because the US Patent and the instant application are drawn to synthetic peptides or analogs encoding an immunogenic transferrin receptor protein from *Haemophilus* between 6 and 150 amino acids or comprising SEQ ID NO:74.

The instant claims of 10/043,344 are drawn to an immunogenic composition comprising a synthetic peptide having no less than six amino acids and no more than 150 amino acids and containing an amino acid sequence corresponding to a portion of a transferring receptor protein of a strain of bacteria or an analog of the transferrin receptor protein and a pharmaceutically acceptable carrier with at least one active component producing an immune response when administered to a host.

The claims of 5,922,562 are drawn to isolated and purified nucleic acid molecule encoding a fragment of a transferring receptor protein of a strain of *Haemophilus* having only an amino acid sequence selected from the group including sequences with between 6 and 150 amino acids such as SEQ ID NO:13-85 and specifically SEQ ID NO: 74 which encode an immunogenic truncated analog of a transferrin receptor protein selected from the group consisting of Tbp1 and Tbp2 proteins from a strain of *Haemophilus* just as the instant claims recite. However the instant claims do not recite using the peptides in an immunogenic composition.

Loosmore et al., WO 96/40929 teach the encoding of immunogenic truncated analog of a transferrin receptor of a strain of *Haemophilus influenzae* as well as associated amino acid sequences (page 5 lines 8-22). The truncated analogs of transferrin receptor proteins are truncated from the C-terminus and include DNA sequences encoding amino acid sequence SEQ ID NO:74 or analog sequences (page 6 lines 10-30). The immunogenic truncated Transferrin Binding Protein 2 (Tbp2) of *Haemophilus* as shown in Figure 31 (page 7 lines 25-32). Table 8 teaches the expression of specific truncated *Haemophilus influenzae* Eagan strain recombinant Tbp2 clones which comprise truncated analogs from Tbp2. Also taught are immunogenic compositions with at least one active component selected from a peptide from a strain of *Haemophilus*, and a pharmaceutically acceptable carrier wherein one component produces an immune response (pages 7-8 lines 32-6).

Thus, the truncated transferrin receptor proteins of the instant application encompass the same truncated transferrin receptor proteins and compositions as recited by the US Patent in view of Loosmore et al. Therefore the immunogenic compositions comprising the peptides are not patentably distinct from the patent, because both encompass the same immunogenic truncated transferrin receptor proteins.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless-
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 14 and 18-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Holland et al.

The claims are drawn to an immunogenic composition comprising a synthetic peptide having no less than six amino acids and no more than 150 amino acids and containing an amino acid sequence corresponding to a portion of a transferrin receptor protein of a strain of bacteria or an analog of the transferrin receptor protein and a pharmaceutically acceptable carrier with at least one active component producing an immune response when administered to a host. The dependant claims are drawn to particular *Haemophilus* strains.

Holland et al., teach evidence for *in vivo* expression of transferrin binding proteins in *Haemophilus influenzae* type b. The transferrin receptor consists of at least two iron-regulated outer membrane transferrin binding proteins (Tbp) (abstract). One protein, Tbp1, has a molecular mass of 100 kD and the other, Tbp2, has a molecular mass of 60-90 kD (abstract). Similar proteins have been found in *Neisseria meningitidis* (page 2986 para.1). The existence of shared antigenic domains of the Tbps of *Haemophilus influenzae* and *Neisseria meningitidis* is known and antibodies to *Haemophilus* are known to cross-react with those of *Neisseria meningitidis* (page 2990

para. 3). Iron acquisition from transferrin is likely to contribute to the virulence by facilitating the growth of *Haemophilus* (page 2987 para. 1). Also, infected humans and animals make antibodies to Tbp's of *Haemophilus* (page 2987 para.1). The materials and methods section teaches preparation of the outer membrane and the isolation of the Tbp's. The organism used was non-typeable *H. influenzae* type b strain Eagan (page 2987). Affinity purification steps isolated a 76 kD and 90 kD Tbp (page 2987-2988 para. 9 and Figure 1). The 76 kD protein may represent a partially unfolded form of the 90 kD protein (page 2990 para. 1) or a truncated form. A humoral immune response to the *Haemophilus* Tbp peptides was observed in rats (page 2988 para. 5). Figure 5 shows that antibodies to both the 76 kD and 90 kD Tbp were elicited during infection of rats (page 2988 para. 5). Holland et al., have also isolated mutants with insertions in genes (page 2990 para. 1).

It is noted that a pharmaceutically acceptable carrier reads on water and therefore would be inherent in composition based on the rats' humoral response. Since the Patent Office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art reference, the burden is upon the applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Thus, Holland et al., teach an immunogenic composition comprising a synthetic peptide having no less than six amino acids and no more than 150 amino acids and containing an amino acid sequence corresponding to a portion of a transferrin receptor

protein of a non-typeable *Haemophilus influenzae* type b, Eagan strain or an analog of the transferrin receptor protein and a pharmaceutically acceptable carrier with at least one active component producing an immune response when administered to a host.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schryvers (US Patent 5, 141,743) in view of Gerlach et al. The claims are drawn to an immunogenic composition comprising SEQ ID NO:74.

Schryvers teach isolating and purifying transferrin receptor proteins from bacterial pathogens and to vaccines containing transferrin-receptor proteins. The transferrin receptors in human pathogens can be from *Neisseria species, Haemophilus influenzae* and *Branhamella catarrhalis* (col. 4 lines 47-64). The invention provides for a transferrin receptor vaccine comprising a transferrin receptor protein isolated from a bacterium or organism expressing the protein or a synthetic peptide whose amino acid sequence is based on the amino acid sequence of a purified transferrin receptor protein or on the nucleotide sequence of a cloned receptor (col. 3 lines 57-68). The preparation may be suspended in a reagent and include an adjuvant (col. 4 lines 1-5). However

Schryvers does not teach the use of SEQ ID NO:74 as being comprised within the immunogenic composition.

Gerlach et al., teach several bacteria including *Actinobacillis (Haemophilus) pleuropneumoniae, Neisseria species, Haemophilus influenzae,* and *Pasturella haemolytica* all use the transferrin of their host as their only source of iron (page 3253). The ability to use the host iron correlates with the binding of transferrin by the iron-starved cells (page 3253). The authors state that the cloning of a gene encoding transferring-binding protein from *A. pleuropneumoniae* was shown by Southern blotting along with other analogous genes from several different serotypes (page 3253). The authors deduced the amino acid sequences and determined which type of transferrin-binding proteins occur in the *A. pleuropneumoniae* type strains (page 3253). Figure 1 shows the nucleotide sequence and the deduced amino acid sequence of the transferrin-binding protein. The disclosed amino acids are identical to SEQ ID NO:74.

Therefore, it would have been prima facie obvious at the time of applicants invention to have used known synethtic peptides within an immunogenic compositons and modify the composition to include the SEQ ID NO:74 because Gerlach et al., teach that it is well known in the art to make and use immunogenic compostion comprising SEQ ID NO:74 as the synthetic peptide or an analog of the transferrin receptor protein and a pharmaceutically acceptable carrier with at least one active component producing an immune response when administered to a host. The transferrin peptide sequences are well known in the art to induce an immune repsone, thus one would have a reasonable expectation of success since no more than routine skill would have been

required to use peptide when the art teaches that immunogenic compositions containing synthetic peptides are known in the art to invoke an immune response in a host and even be protective. Moreover, no more than routine skill would have been required to modify the well known composition by simply incorporating alternative and equivalent antigenic products for the purpose of inducing an immune response a subject.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines JH
September 27, 2004

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